

DOCKET NO: PHRM0041-100/00125US1
Serial No.: 09/838,028

PATENT
FILED: APRIL 19, 2001

REMARKS

Claims 1-29, 31, and 34-89 were pending in the application. Claims 1-29 and 36-81 were withdrawn from consideration as directed to non-elected inventions. Claims 1-29, 34, 36-81, 85, and 86 have been canceled. Claims 31 and 87 have been amended. Upon entry of this amendment claims 31, 35, 82-84, and 87-89 will be pending.

No new matter has been added.

Rejection under 35 U.S.C. § 101

Claims 31, 35, 35, and 82-89 remain rejected under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by a specific, substantial and credible asserted utility or a well established utility. The Office alleges that the arguments presented by Applicants in response to the previous Office Action, although considered, were not deemed persuasive. Applicants disagree and request reconsideration of the rejection.

The Utility Examination Guidelines (the "Guidelines") require that a claimed invention have a specific, substantial and credible asserted utility, or, alternatively, a well-established utility. As Applicants have asserted utilities that are specific, substantial and credible, and well established, the Utility Requirement has been satisfied. Applicants, therefore, respectfully request the withdrawal of the rejection under 35 U.S.C. § 101.

Under the Guidelines, Office personnel are instructed to review the specification and claims of the application to determine if a specific and substantial utility that is credible is present. The Guidelines note that the specific and substantial requirement "excludes 'throw-away', insubstantial, or 'nonspecific' utilities, such as the use of a complex invention as landfill." The Guidelines go on to note that an Examiner's "*prima facie* showing *must* establish that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial." "If the applicant has asserted that the claimed invention is useful for any particular practical purpose (*i.e.*, it has a 'specific and substantial utility') and the

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assertion would be considered credible by a person of ordinary skill in the art, do *not* impose a rejection based on lack of utility." (Guidelines, emphasis added).

The Guidelines also comment on the use of computer based analysis of nucleic acids to assign functions to a nucleic acid or polypeptide based upon homology to sequences found in databases. Specifically, the Guidelines state that the:

suggestions to adopt a *per se* rule rejecting homology based assertions of utility *are not adopted*. An applicant is entitled to a patent to the subject matter claimed unless statutory requirements are not met (35 U.S.C. 101, 102, 103, 112) . . . The inquiries involved in assessing utility are fact dependent, and the determinations must be made on the basis of scientific evidence. Reliance on the commenters' *per se* rule, rather than a fact dependent inquiry, is impermissible because the commenters provide no scientific evidence that homology-based assertions of utility are inherently unbelievable or involve implausible scientific principles. See, e.g., *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (rejection of claims improper where claims did 'not suggest an inherently unbelievable undertaking or involve implausible scientific principles' and where "prior art * * * discloses structurally similar compounds to those claimed by the applicants which have been proven * * * to be effective').

A patent examiner *must* accept a utility asserted by an applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. The examiner's decision must be supported by a preponderance of all the evidence of record. *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). More specifically, when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565, 39 USPQ2d 1895, 1900 (Fed. Cir. 1996). The Office will take into account both the nature and degree of the homology.

When a class of proteins is defined such that the members share a specific, substantial, and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein. If the preponderance of the evidence of record, or of sound scientific reasoning, casts doubt upon such an asserted utility, the examiner should reject the claim for lack of utility under 35 U.S.C. 101. For example, where a class of proteins is defined by common structural features, but evidence shows that the

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members of the class do not share a specific, substantial functional attribute or utility, despite having structural features in common, membership in the class may not impute a specific, substantial, and credible utility to a new member of the class. When there is a reason to doubt the functional protein assignment, the utility examination may turn to whether or not the asserted protein encoded by a claimed nucleic acid has a well-established use. If there is a well-established utility for the protein and the claimed nucleic acid, the claim would meet the requirements for utility under 35 U.S.C. 101. If not, the burden shifts to the applicant to provide evidence supporting a well-established utility. There is no *per se* rule regarding homology, and each application must be judged on its own merits.

(Guidelines; emphasis added).

Preliminarily, Applicants remind the Office that specific and substantial utilities have been provided for the claimed polypeptides. The asserted utilities are credible to one of skill in the art. The Office has failed to provide any evidence that "it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial."

It appears that the Examiner's assertion that the claimed invention lacks utility may have been based upon the often-repeated examples of "throwaway" utilities, including the use of a genetically modified mouse as snake food or of the use of uncharacterized compositions as "landfill" or as shampoo ingredients. Such assertions focus on the non-specificity of such uses. For example, anything that a snake could arguably fit within its mouth could serve as food for the snake. Likewise, anything that could fit in a landfill could be a landfill component. Virtually any substance that can be dissolved in a shampoo could be used a shampoo ingredient. An important issue raised by the fact that any substance could be so used is that the substance may be wholly inappropriate for the asserted utility. In the context of a shampoo ingredient, the added substance may be highly caustic and cause serious burns to the skin. This scenario supports the logical conclusion that a "candidate" should be appropriate for the utility asserted. Further, to be "appropriate for use", the substance cannot be uncharacterized. Without characterization one cannot determine whether the substance is appropriate for the asserted utility.

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The use of such uncharacterized substances for purposes of dubious worth stands in sharp contrast to the present invention. As recited in Applicants' previous response, the pending claims recite a *specific* polypeptide, *i.e.*, Con-218. Through several rounds of analysis, the claimed polypeptide was shown to be a GPCR. The polypeptide was further shown to be related to a putative G protein-coupled receptor from Japanese medaka (*see* page 79 of the application as filed, lines 9-15). The nucleotide and amino acid sequences of Con-218 and Con-218-RN rat) are provided as SEQ ID NO:1 and SEQ ID NO 3 (nucleotide) and SEQ ID NO:2 and SEQ ID NO: 4 (amino acid). Specific expression profiles for the Con-218 polypeptide are provided in Example 5. Such polypeptides are useful, *inter alia*, for generating antibodies, identifying ligands or protein partners, evaluating expression patterns, evaluating protein activity, etc. As set forth in Example 5, the claimed polypeptides also:

have utility for treating neurological disorders, including but not limited to, schizophrenia, affective disorders, ADHD/ADD (*i.e.*, Attention Deficit-Hyperactivity Disorder/Attention Deficit Disorder), and neural disorders such as Alzheimer's disease, Parkinson's disease, migraine, and senile dementia. Some other disease for which modulators of Con-218 may have utility include depression, anxiety, bipolar disease, epilepsy, neuritis, neurasthenia, neuropathy, neuroses, metabolic and cardiovascular diseases and disorders (*e.g.* type 2 diabetes, obesity, anorexia, dyslipidemias, hypertension, and the like.)

Use of Con-218 modulators, including Con-218 ligands and anti-Con-218 antibodies to treat individuals having such disease states is intended as an aspect of the invention.

It is clear, therefore, the claimed polypeptide is neither the equivalent of the uncharacterized complex invention used as "landfill" nor of a caustic substance used in a shampoo.

The Examiner compares the claimed invention to, *inter alia*, a "molecular weight marker/calibration standard", or a source of heat or light through combustion. The Examiner goes on to say that "to accept Applicant's arguments that any nucleic acid encoding any protein of human origin is useful as a marker would be comparable to conceding that any object of fixed mass has *prima facie* utility as a weight standard, irrespective of any other properties possessed by that object." Also, the Office alleges

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that if Applicants' assertions were followed, "any item having a constant mass within an acceptable range can be used to calibrate a produce scale in a grocery store" and that this was "irrespective of any other properties possessed by that object." (Office Action, page 4).

As discussed above, the Office, through its analogy, appears to imply that the claimed polypeptides are wholly unsuitable for the asserted utilities; i.e. because wholly unsuitable objects *could* be used for purposes not specific to the object. For example, *anything* could be used to calibrate a grocery scale. Applicants agree that there are numerous objects which *could* be used to calibrate a grocery scale but, for any number of reasons, many of such objects may be inappropriate or unsuited for that utility. Applicants note, however, that the Office has failed to provide any reason why the claimed polypeptides are inappropriate or unsuited for the several asserted utilities. Applicants remind the Examiner that the utilities asserted for the claimed polypeptide are not "irrespective of any other properties possessed by that object."

Applicants again note that the claimed invention has substantial and specific utilities that are credible, in contrast to the use of any (even uncharacterized) objects as calibration standards. Notwithstanding the Office's arguments regarding unsubstantial or nonspecific utilities of calibration standards, *inter alia*, Applicants assume, however, that the Office recognizes that objects including calibration standards, *when appropriate for use*, are patentable. Indeed, upon a cursory review of patents listed on the PTO's website, Applicants found numerous patents issued with claims directed to, *inter alia*, calibration standards. For example, United States Patent 6,646,737, issued November 11, 2003, claims a calibration standard. Similarly, United States Patents 6,356,069 and 6,174,728 also claim calibration standards. Applicants have provided evidence, including several different homology comparisons and expression analysis, that the claimed polypeptides are suitable for use as GPCRs.

The Office further makes the assertion that granting Applicants:

a patent encompassing an isolated polynucleotide encoding a naturally occurring human protein of as yet undetermined biological significance, or the protein encoded thereby, would be to grant Applicant a monopoly "the

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metes and bounds' of which 'are not capable of precise delineation.' That monopoly 'may engross a vast, unknown, and perhaps unknowable area' and 'confer power to block off whole areas of scientific development, without compensating benefit to the public.

(Office Action, page 5 (citing *Brenner v. Manson*)).

Applicants respectfully assert that the Office has mischaracterized the *Brenner* decision. Applicants first note that the pending claims are not directed to processes but instead to compositions. The Office apparently failed to consider the entirety of the first sentence cited from *Brenner*. The sentence in its entirety states "Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation." The equivalent of the "product" discussed in *Brenner* is the claimed polypeptide. As discussed in length above, many utilities have been asserted for the claimed polypeptides. None of the asserted utilities are incredible or have dubious worth. The polypeptide claimed by Applicants has a defined structure (*i.e.*, having at least 95% homology to SEQ ID NO: 2 and/or SEQ ID NO: 4 or a polypeptide that is encoded by a polynucleotide that hybridizes to SEQ ID NO: 1 and/or SEQ ID NO:3 under specific hybridization conditions). The metes and bounds of Applicants' invention are, therefore, readily determinable.

Further, Applicants note that rejections of claims based on the "metes and bounds" of the claim are properly made under 35 U.S.C. § 112, second paragraph. Applicants respectfully assert that the art-skilled would readily comprehend the "metes and bounds" of the presently claimed Con-218 polypeptides.

Applicants note that only a "substantial likelihood" of utility need be provided; certainty is not required. *Brenner*, 383 U.S. at 532. The amount of evidence required to prove utility depends on the facts of each particular case. *In re Jolles*, 628 F.2d 1322, 1326 (CCPA 1980). "The character and amount of evidence may vary, depending on whether the alleged utility appears to accord with or to contravene established scientific principles and beliefs." *Id.* Unless there is proof of "total incapacity," or there is a "complete absence of data" to support the applicant's assertion of utility, the utility requirement is met. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555,

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1571 (Fed. Cir. 1992); *Envirotech*, 730 F.2d at 762. The Office has failed to provide proof of "total incapacity". Applicants have provided data that supports the asserted utilities. Accordingly the utility requirement has been met.

Although Applicants assert that specific and substantial utilities that are credible have been provided for the claimed invention, Applicants also note that the Utility requirement may also be satisfied by an "Art Established Utility" which means that "a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention . . . and the utility is specific, substantial and credible." (M.P.E.P. §2107). Well-established, art established utilities exist for the claimed polypeptides of the present invention.

To support Applicants' assertion that there is an "Art Established Utility," Applicants point out that commercial products relating to GPCRs for which no *confirmed* function has been identified are commercially available. GPCRs, ORF clones of GPCRs, and antibodies that bind to GPCRs are commercially available. For example, Applicants point out that FabGennix Inc. of Shreveport, Louisiana sells an antibody directed to Retinal Anti-GP75. GPCR75 is said to be a GPCR for which a ligand has not yet been identified (*see* attached product sheet). Invitrogen sells ORF clones of GPCRs including those for which a ligand has not yet been identified (*see* attached list, especially noting Clone Ids IOH22483, IOH14039, IOH13056, IOH22637, IOH13239, and IOH13516). MD Bio of Taiwan sells GPCR peptides and antibodies against such peptides, again where no ligand has yet been identified. That at least three companies make and sell such GPCR products proves that there is an art-established utility for the presently claimed GPCR polypeptides. Applicants note that it is an industry standard to develop such products before confirmation of a function. Accordingly there could be no better proof of the utilities of the claimed polypeptides- such products are made by a manufacturer (who expects to sell them) for consumers (who expect to buy them). Any argument that there is no art-recognized utility for such polypeptides, and the polynucleotides that encode them, seems meritless. If the Patent Office is aware of any evidence which would support the Office substituting its judgment for the practices of the industry, Applicants

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respectfully request that an affidavit stating the basis of this evidence be placed on the record.

In summary, a patent examiner *must* accept a utility asserted by an applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. The Guidelines make clear that when a patent application claiming a nucleic acid, for example, asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility *must* be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. The Office has failed to provide any evidence, less still a preponderance of the evidence, to cast doubt upon any of the asserted utilities. The Office has also failed to provide any evidence that the asserted utilities are "throwaway utilities" or that the claimed polypeptides are inappropriate or unsuited for the several asserted utilities. Finally, even assuming *arguendo* that the asserted utilities are not specific or substantial, the art established utilities for the claimed polypeptides satisfy the Utility requirement of § 101.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be withdrawn upon reconsideration.

Rejections under 35 U.S.C. § 112

Claims 31, 34, and 35, and 82-89 remain rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to adequately teach how to use the instant invention for the reasons that the Office gave with regard to the rejection of these claims under 35 U.S.C. § 101. As discussed above, the present invention *is* supported by a specific, substantial, and credible asserted utility as well as a well-established utility. Accordingly, Applicants respectfully request that the rejection be withdrawn.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

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Claims 87-89 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly vague and indefinite. The Office alleges that the phrase “‘stringent hybridization conditions’ is conditional and a single defining set of conditions is not recited in either the claims or the instant specification” (Office Action, page 7). Applicants respectfully disagree.

The phrase “stringent hybridization conditions” is well known to the art skilled and, as acknowledged by the Office, is defined in the instant specification. Notwithstanding the foregoing, however, Applicants have amended claims 87- 89 to incorporate the specific hybridization conditions as set forth in the present application (see, page 15, lines 4-8).

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

Rejection under 35 U.S.C. § 102

Claims 30, 35, and 82-86 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Dohlman *et al.* (*Biochemistry*, 27(6):1813-1817 (1998), hereinafter the “Dohlman reference”). According to the Office, the Dohlman reference discusses a sequence comprising a fragment of SEQ ID NO: 2 or SEQ ID NO:4.

Preliminarily, Applicants note that claim 31 has been amended. As amended claim 31 no longer recites fragments of SEQ ID NO: 2 or SEQ ID NO: 4.

The Dohlman reference discusses the identification and sequence of a binding site peptide of the β_2 -Adrenergic Receptor. The Dohlman reference does not discuss or even suggest a polypeptide comprising SEQ ID NO:2 or SEQ ID NO:4. Therefore, the Dohlman reference fails to teach each and every limitation of the claim. Accordingly, the Dohlman reference does not anticipate the present invention.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

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Claims 31, 34, 35, 82-89 remain rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Gan *et al.* (U.S. Patent Publication 2002/0100067 A1). According to the Office, Applicants were not granted the benefit of the filing date of an earlier filed application under 35 U.S.C. § 119(e) because the application allegedly does not meet the requirements under 35 U.S.C. § 112, first paragraph. Applicants respectfully disagree.

The priority document for the present application is a provisional application (U.S. Ser. No. 60/198,600). According to the M.P.E.P., "The filing date of a provisional application is the date on which (1) a specification which complies with 35 U.S.C. 112, first paragraph, and (2) any drawing required by 37 C.F.R. 1.81(a) are filed." (M.P.E.P. § 201.04(b)). U.S. Ser. No. 60/198,600 complies with these requirements and contains a written description of the invention, how to make and use the invention, and the best mode by which to use the invention. There is nothing in the M.P.E.P., the Federal Laws, or the C.F.R. that suggests or recites that the utility requirement must be satisfied in the provisional application. Notwithstanding the foregoing, Applicants note that for at least the reasons discussed above in respect to the present application, the priority document also complies with the requirements under 35 U.S.C. § 101.

The specification of the provisional application recites how to make the polypeptide and how to use the polypeptide in the development of antibodies. The antibodies can be used to analyze protein expression in cells, tissues, or other samples that contain proteins, such as a cell lysate. The priority document also discloses how to identify binding partners for the polypeptide. Furthermore, the priority application provides a written description of the polypeptide. Therefore, the earlier filed application complies with the requirements of 35 U.S.C. § 112, first paragraph.

Accordingly, the Gan reference is not available as a reference under 35 U.S.C. § 102(c) since its publication date is after the filing date of the present application. In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 102(e) be withdrawn.

Withdrawn Claims

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The Office notes that the instant application contains withdrawn claims directed to non-elected inventions and requires cancellation of the withdrawn claims. Applicants have canceled the claims previously withdrawn without prejudice to future presentation in related applications.

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Conclusion

Applicants believe the claims are in condition for allowance. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (215) 665-6928 to clarify any unresolved issues raised by this response.

Respectfully submitted,



Daniel M. Scolnick, Ph.D.
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DATE: December 15, 2003

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Philadelphia, PA 19103-3508
Telephone: (215) 665-2000
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Attachments: Product Sheet for Anti-GPCR-75 Antibodies
Product sheet for GPCR control peptides and antibodies (MD Bio)
Product sheet for GPCR ORF clones (Invitrogen)

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Buy	Clone ID	Species	Definition	Gene Symbol
<input type="checkbox"/>	IOH329A	Human	complement component 5 receptor 1 (C5a ligand); complement component-5 receptor-2 (C5a ligand)	CSR1
<input type="checkbox"/>	IOH12614	Human	purinergic receptor P2Y, G-protein coupled, 11	P2RY11
<input type="checkbox"/>	IOH22483	Human	clone MGC:33224 IMAGE:5267661, mRNA, complete cds.	RDC1
<input type="checkbox"/>	IOH14039	Human	Similar to putative nuclear protein ORF1-FL49	ORF1-FL49
<input type="checkbox"/>	IOH11464	Human	glycoprotein Ib (platelet), alpha polypeptide	GP1BA
<input type="checkbox"/>	IOH11967	Human	tachykinin receptor 1 isoform short; NK-1 receptor; Tachykinin receptor 1 (substance P receptor; neurokinin-1 receptor); tachykinin 1 receptor (substance P receptor; neurokinin 1 receptor); neurokinin 1 receptor	TACR1
<input type="checkbox"/>	IOH13056	Human	similar to POSSIBLE GUSTATORY RECEPTOR CLONE PTE01	LOC11513
<input type="checkbox"/>	IOH9916	Human	coagulation factor II (thrombin) receptor-like 1	F2RL1
<input type="checkbox"/>	IOH9624	Human	vasoactive intestinal peptide receptor 2	VIPR2
<input type="checkbox"/>	IOH10679	Human	endothelin receptor type A	EDNRA
<input type="checkbox"/>	IOH22637	Human	Similar to parathyroid hormone receptor 1, clone MGC:34562 IMAGE:5180855, mRNA, complete cds.	PTHR1
<input type="checkbox"/>	IOH13583	Human	Duffy blood group	FY
<input type="checkbox"/>	IOH4585	Human	cholecystokinin B receptor	CCKBR
<input type="checkbox"/>	IOH11033	Human	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 4; G protein-coupled receptor; LPA receptor EDG4; Lysophosphatidic acid receptor EDG4	EDG4
<input type="checkbox"/>	IOH10866	Human	CD97 antigen isoform 2 precursor; leukocyte antigen CD97; seven-span transmembrane protein	CD97
<input type="checkbox"/>	IOH22632	Human	formyl peptide receptor-like 1; Iipodin A4 receptor (formyl peptide receptor related)	FPR1
<input type="checkbox"/>	IOH22669	Human	adrenomedullin receptor	ADM2
<input type="checkbox"/>	IOH13229	Human	super conserved receptor expressed in brain 3	SREB3

http://orf.invitrogen.com/cgi-bin/ORF_Browser?family=G-Protein+Coupled+Rec 09/03/2003



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Novel Orphan retinal G-protein coupled Receptor (GPCR-75) selective antibodies

Anti-GPCR-75 Antibodies (GPCR75-100P, GPCR75-101AP and GPCR75-112AP)

Recently a novel human G-protein coupled receptor gene has been characterized and mapped to chromosome 2p16. This gene codes for a 540 amino acid protein in retinal pigment epithelium (RPE) and cells surrounding retinal arterioles. In contrast, the Northern blot data obtained from mouse sections suggest the expression of transcripts in photoreceptor inner segments and I outer plexiform layer. The transcripts of the GPCR-75 gene (7kb) are also found in abundance in brain sections. So far, no mutations in GPCR-75 protein were identified in patients suffering from Doyme's honeycomb retinal dystrophy (DHRD), an inherited retinal degeneration disease that maps to chromosome 2p16 (1).

The GPCR-75 protein is approximately 78 kDa (540 amino acids) protein that is primarily expressed in human retinal pigment epithelium (RPEs). The GPCR-75 sequence analyses suggest the presence of 7 trans-membrane domains, a characteristic feature of GPCR. The protein has putative N-glycosylation sites near the extra cellular N-terminal end of the proteins. The protein has a large 3 intra cellular loop which might be the site for interaction of G-proteins. The short carboxy terminal is intracellular and has putative post-translational modification lipid modification sites.

The Anti-GPCR-75-selective antibodies were generated against conserved sequences near N- and C-termini of the protein that are unique to GPCR-75 protein. The polyclonal antibody strongly labels a 78 kDa protein in RPE cell extracts. Anti-GPCR-75-selective antibody is also available in affinity-purified form for confocal, Western blotting and immunocytochemical analyses. *FabGennix Int. Inc.* will also conjugate antibodies with fluorescent probes upon request at extra charge. *FabGennix Int. Inc.* will also provides antibodies against proteins that are involved in retinal degenerative diseases such as various Anti-PDE antibodies, Anti-MERTK, Anti-Phospho-MERTK, EGF-containing fibulin like intracellular protein (EFEMP1), Anti-Myocilin (TIGR), Anti-Bestrophin, Anti-ELVOL4 and a Usher syndrome specific Anti-USH2a antibodies etc. *FabGennix Int. Inc.* employs cyclic peptide methodology for generating antibodies, which results in higher titer and specificity (2). *FabGennix Int. Inc.*, will also provide Western blot positive controls for most of these antibodies in ready-to-use buffer for easy identification of respective proteins. Limited quantities of antigens are also available. Please enquire for their availability before ordering.

Catalog #	Host Species	Nature	Cross reactivity	Quantity	volume	Price
GPCR75-100P	Rabbit	Polyclonal antisera	R, M, H	100 ml	100 ul	\$ 195.00
GPCR75-101AP	Rabbit	Affinity purified IgG	R, M, H	100 ug	150 ul	\$ 225.00
GPCR75-112AP	Rabbit	Affinity purified IgG	R, M, H	100 ug	150 ul	\$ 225.00
PC-GPCR75	N/A	WB positive control	Rat	For 5 App	60 ul	\$ 75.00
P-GPCR75	N/A	Antigenic peptides	n/a	250 ug	Inquire	\$ 65.00

R = rat; M = mouse; H = human; C = chicken; monk = monkey; * not all variants are labeled equally

Immunogen: Synthetic cyclic peptide (GPCR75-101AP = PNATSLHYPHSQEONSTG-amide; GPCR75-112AP = STSLQQLQLHTATLVTC-amide).

Concentration: GPCR75-101AP, GPCR-112AP IgG concentration 0.75-1.25 mg/ml in 50% antibody stabilization buffer.

Applications: Antibody GPCR75-100/GPCR75-101AP are ideal for WB, IEM and IHC assays. The dilutions for this antibody is for reference only, investigators are expected to determine the optimal conditions for specific assay in their laboratory. Dilution: WB > 1:500; Immunoprecipitation & Lip pull-down assays > 1:250

Reactivity: This antibody detects a single 78 kDa Orphan GPCR75 protein in human RPE cell extracts.

Protocols: Standard protocol for various applications (WB; IEM and IHC) of this antibody is provided with the product specification sheet, however, *FabGennix Int. Inc.* strongly recommends investigators to optimize conditions for use of this antibody in their laboratories.

Form/Storage: The antiserum is supplied in antibody stabilization buffer with 0.02% sodium azide or thimerosal/merthiolate as preservative. The affinity-purified antibodies are purified on antigen-agarose affinity column and supplied as 1-1.25 mg/ml IgG in antibody stabilization buffer containing preservatives with low viscosity and cryogenic properties. For long-term storage of antibodies, store at -20°C. Now these antibodies can be stored at -20°C and used immediately with out thawing. *FabGennix Inc.* does not recommend storage of very dilute antibody solutions unless they are prepared in specially formulated multi use antibody dilution buffer (Cat # DiluBuffer). Working solutions of antibodies in DiluBuffer should be filtered through 0.45µm filter after every use for long-term storage.

References:

- Tarttelin E. E., Kriachner L. S., Bellingham J., Baffi J., Taymanas S. E., Gregor E. K., Csaky K., Stratakis C. A., Gregory-Evans C. Y. *Biochem. Biophys. Res. Commun.* 260, 174-180, 1999.
- Farooqui, S. M., Brock, W. J., A. Hamdi, Prasad, C. (1991) *J. Neurochem.* 57, 1363-1369.

* For users who may require large amounts of GPCR75-100P or GPCR75-101AP, please enquire about bulk material discounts.

This Product is for Research Use Only and is NOT intended for use in humans or clinical diagnosis.

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2940 Youree Drive, Suite E, Shreveport, LA 71104



78 kDa Orphan Receptor-75
in human RPE cells.
Antibody GPCR-100P
(1:400)



Rat Taste Receptor 2 (TR2) Antibodies

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Cat. # TR21-P, Rat TR2 Control Peptide # 1, SIZE: 100 ug/100 ul
FORM: CE Soln CE Lyophilized Lot # 3113P

Cat. # TR21-S, Rabbit Anti-rat TR2 antiserum # 1, SIZE: 100 ul neat antiserum
FORM: CE Soln CE Lyophilized. Lot # 38889S

Cat. # TR21-A, Rabbit Anti-rat TR2 Ab # 1 (affinity pure) SIZE: 100 ug
FORM: CE Soln CE Lyophilized. Lot # 38889A

Higher vertebrates are believed to possess at least five basic tastes: Sweet, bitter, sour, salty, and unami (the taste of monosodium glutamate). Taste receptor cells that may selectively reside in various parts of the tongue and respond to different tastants and perceive these taste modalities. Circumvallate papillae, found at the very back of the tongue, are particularly sensitive to bitter substances. Foliate papillae, found at the posterior lateral edge of the tongue, are sensitive to sour and bitter. Fungiform papillae at the front of the tongue specialize in sweet taste.

Recently, two novel taste receptors, TR1 and TR2, have been cloned with distinct topographical distribution in taste receptor cells and taste buds. TRs are members of a new group of 7 TM domain containing GPCR distantly related to other chemosensory receptors (Ca²⁺-sensing receptor (CaSR, a family of putative hormone receptor (V2R), and metabotropic glutamate receptors). TR1 is expressed in all fungiform taste buds, whereas TR2 localized to the circumvallate taste buds. Both receptors do not co-localize with gustducin.

Source of Antigen and Antibodies

TR1 (rat 840 aa) and TR2 (rat 843 aa) share ~40% homology with each other, and ~30% with CaSR, and 22-30% with V2R pheromone receptors and mGLURs. Rat TR are 7 TM domain containing protein with an extra long N-terminal, extracellular domain (1). A 19 AA Peptide (designated TR21-P; control peptide) sequence near the C-terminus of rat TR2(1) was selected for antibody production. The peptide was coupled to KLH, and antibodies generated in rabbits. Antibody has been affinity purified using control peptide-Sepharose.

Form & Storage

Control peptide Solution is provided in PBS, pH 7.4 at 1 mg/ml (100 ug/100 ul). Antiserum is supplied as neat serum (100 ul soln or lyophilized). Affinity pure antibodies were purified over the peptide-Sepharose column and supplied as 1 mg/ml soln in PBS, pH 7.4 and 0.1% BSA as stabilizer (100 ul in solution or Lyophilized).

The peptides and antibodies also contain 0.1% sodium azide as preservative. Lyophilized products should be reconstituted in 100 ul water and gently mixed for 15 min at room temp. All peptide/antibody

<http://www.mdhkn.com/tw/Ab-1/tr21.html>

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received in solution or

reconstituted from lyophilized vials should be stored frozen at -20°C or below in suitable aliquots. It is not recommended to store diluted solutions. Avoid repeated freeze and thaw.

Recommended Usage

Western Blotting (1:1K-5K for neat serum and 1-10 ug/ml for affinity pure antibody using ECL technique).

ELISA: Control peptide can be used to coat ELISA plates at 1 ug/ml and detected with antibodies (1:10-50K for neat serum and 0.5-1 ug/ml for affinity pure).

Histochemistry & Immunofluorescence: We recommend the use of affinity purified antibody at 1-20 ug/ml in paraformaldehyde fixed sections of tissues (1).

Specificity & Cross-reactivity

The 19 AA rat TR21-P control peptide is specific for rat TR2. It has no significant sequence homology with TR1 or gustducin or pheromone receptors. Antibody cross-reactivity in various species has not been studied. The TR21-P control peptide is available to confirm specificity of antibodies.

References:

1. Hoon MA et al (1999) Cell 96, 541-555; Lindemann B (1999) Nature Med. 5, 381-382

"N at Antisera" are the unpurified antiserum and it is suitable for ELISA and Western.
"Affinity pure" antibodies have been over the antigen-affinity column and recommended for immunohistochemical applications.

"Control peptides" can not be used for Western as they are very short peptides. They are intended for ELISA or antibody competition studies.

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